Applicants submit herewith as **Exhibit A** a substitute specification as requested by the Examiner in the April 12, 2000 Interview Summary. The substitute specification includes all of the amendments that were previously submitted. Claim 2 has been amended to make reference to 'at least about 70% homology' to the sequence shown in SEQ ID NO:5. This amendment is supported on page 24, lines 3-4 of the subject specification as originally filed.

Applicants acknowledge with appreciation the Examiner's statement that the specific sequences of SEQ ID NOS:5 and 6 are free of the prior art. In view of the Examiner's statement, new claims 89 and 90, directed to the nucleic acid of SEQ ID NO:5 and a nucleic acid encoding the amino sequence of SEQ ID NO:6 respectively, have been added and are believed to be allowable. No new matter is added by these claims. Applicants maintain that the amendments and new claims raise no issue of new matter.

Claims 2, 6, 48-52, 55, 56, 61-64, 83-85, 89 and 90 will be pending and under examination upon entry of this amendment.

Restriction/Election Requirement

Applicants acknowledge with appreciation the Examiner's statement in the Office Action mailed March 29, 2000 that Applicant's arguments against the restriction requirement mailed 11 November 1999 has been fully considered and was deemed persuasive. The Examiner stated that Applicants elected CD86 as the species to be examined in the instant application and that non-elected species CD80 would be considered only in those claims involving CD86/CD80 fusion proteins. Accordingly, the restriction requirement has been withdrawn and claims 2, 6, 46-52, 55, 56, 61-64 and 83-88 are to be

prosecuted on the merits.

Objections to the Specification

In the Office Action mailed March 29, 2000, the Examiner stated that a new title is required that is clearly indicative of the invention to which the claims are directed. The title has been amended accordingly.

In addition, the Examiner stated that the table in the specification at page 44, lines 23-37 and continued on page 45, lines 1-2 is indecipherable due to problems with the character alignment and required its connection. The table in the specification has been corrected in order to clarify the character alignment in the substitute specification attached hereto as **Exhibit A**. The substitute specification is submitted in response to the April 12, 2000 Interview Summary and incorporates the amendments previously submitted. Applicants attach hereto as **Exhibit B** a statement signed by the undersigned averring that the substitute specification contains no new matter.

Rejections Under 35 U.S.C. §112, first paragraph

The Examiner set forth two rejections under 35 U.S.C. § 112, first paragraph. Applicants traverse each of these rejections and maintain that the claimed subject matter is described in such a way as to enable one skilled in the art to make and/or use the invention.

I. **Rejection Of Claims 2, 46, 47 and 83**

The Examiner rejected claims 2, 46, 47, and 83 under 35 U.S.C. § 112, first paragraph, alleging that there is no written description of "genomic DNA" in the specification. Claims 46 and 47 have been canceled, and claim 2 (from which claim 83 depends) has been amended to encompass nucleic acid sequences that are at least 70% homologous with the cDNA of SEQ ID NO:5. Such nucleic acid sequences are fully described by the specification. For example, the specification recites that:

> [T]he present invention also encompasses feline CD80, CD86, CD28 or CTLA-4 DNAs (and polypeptides) derived from other feline species, including without limitation domestic cats, lions, tigers, cheetahs, bobcats and the like. Feline CD80, CD86, CD28 or CTLA-4 homologues of the sequence shown in Figures 1 to 5 are easily identified by screening cDNA or genomic libraries to identify clones that hybridize to probes comprising all or part of the sequence of Figures 1 to 5. Alternatively, expression libraries are screened using antibodies that recognize feline CD80, CD86, CD28 or CTLA-4. Without wishing to be bound by theory, it is anticipated that CD80 or CD86 genes from other species will share at best about 70% homology with the feline CD80, CD86, CD28 or CTLA-4 genes.

See specification (as originally filed) at page 23, line 28 to page 24, line 4. The application provides an example of such a nucleic acid, e.g., the nucleic acid shown in Figure 3A. Indeed, the application provides the reader with the sequences of specific PCR primers that can be used to isolate the whole CD86 gene (see page 39, lines 23-27 of the specification as originally filed).

II. Rejections of Claims 2, 87 and 88

The Examiner rejected claims 2, 87 and 88 under 35 U.S.C. § 112, first paragraph, alleging that the specification does not provide adequate written description for the claimed invention because, in the Examiner's view, there are two possible interpretations of the claims: that the vector codes for both nucleic acids and two individual protein products are obtained from one vector, or that the nucleic acids are fused to code for one fusion protein. Claims 87 and 88 have been canceled. As to claim 2, it is believed that this claims may have been included in this rejection in error, as claim 2 sets forth only one nucleic acid sequence, and thus the stated basis for the rejection does not appear to apply to claim 2.

In view of these comments and amendments, reconsideration and withdrawal of these grounds of rejection are respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner set forth four rejections under 35 U.S.C. § 112, second paragraph. Applicants traverse each of the rejections and maintain that the claimed invention is fully described and distinctly claimed.

I. Rejection of Claims 2, 55 and 86

The Examiner alleges that claims 2, 55 and 86 are indefinite in that they only describe "the composition" by an arbitrary name. The Examiner asserts that Applicant should particularly point out and distinctly claim the "protein molecule and variant thereof" by

claiming characteristics associated with the protein (e.g. activity, molecular weight, amino acid composition, N-terminal sequence, etc.).

Applicants maintain that the claims are definite as originally written. Claim 2 recites "an isolated nucleic acid encoding a feline CD86 ligand or a feline soluble CD86 ligand." Applicants point out that the language "protein molecule and variant thereof" as called out by the Examiner on page 4 of the Office Action is not present in the pending claims. The pending claims clearly refer to the ligand "feline CD86." Nevertheless, Applicants have amended claim 2 to include the phrase "wherein the nucleic acid is at least about 70% homologous with the nucleic acid shown in SEQ ID NO: 5," thereby including a sequence characteristic as part of that claim, and of claim 55, which depends therefrom. Claim 86 has been canceled.

II. Rejection of Claims 2, 46, 47 and 83

The Examiner rejected claims 2, 46, 47, and 83, asserting that the metes and bounds of what is included in the "genomic DNA" of the instant application is unclear. Specifically, the Examiner stated that it is not clear what introns, exons and regulatory elements are to be considered part of the "genomic DNA."

Claims 46 and 47 have been canceled. Neither claim 2 nor claim 83 contain the term "genomic DNA," so it is not understood how this rejection applies to them and it is believed that claims 2 and 83 may have been included in this rejection in error.

III. Rejection of Claims 2, 87 and 88

The Examiner alleges that claims 2, 87 and 88 are indefinite because it is unclear if the nucleic acid sequence of SEQ ID:5 and SEQ ID:1 are to be placed in the same vector with two different promoters, allowing for expression of two separate proteins in one vector, or whether the two sequences can be fused to each other and expressed as one protein.

While Applicants disagree with the Examiner's position, in order to expedite prosecution, claims 87 and 88 have been canceled. As to claim 2, again, it is not clear why this claim has been included in this rejection, because claim 2 is not directed to a vector and thus the stated basis for rejection does not appear to apply to claim 2.

IV. Rejection of Claims 2, 55 and 86

The Examiner rejected claims 2, 55 and 86, alleging that it is unclear whether the vector in question contains the nucleotide sequence of CD80 or CD86.

Claim 2 is directed to a nucleic acid that encodes feline CD86. Claim 55 depends from claim 2 and is directed to a vector comprising the nucleic acid of claim 2. Claim 86 (which has been canceled) depends from claim 55 and further comprises a nucleic acid encoding feline CD80. Therefore, in reply to the Examiner's query, claim 2 and claim 55 are directed to a nucleic acid encoding feline CD86, and vectors that comprise a nucleic acid encoding feline CD86. Claim 86 is directed to a vector that, in addition to a nucleic acid encoding feline CD86, also comprises a nucleic acid

encoding feline CD80. Thus, Applicants maintain that these claims particularly point out and distinctly claim the present invention.

In view of these amendments and arguments, reconsideration and withdrawal of these grounds of rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

I. Rejection of Claims 2, 6, 46-52, 55, 56, 61-64 and 83-85

Claims 2, 6, 46-52, 55, 56, 61-64, and 83-85 are rejected under 35 U.S.C. § 103(a) as unpatentable over Freeman et al. (U.S. Patent No. 5,942,607) ("Freeman et al.").

The Examiner stated that Freeman et al. teach the human B7-2 (CD86) nucleic acid and amino acid sequence, as well as inserting the CD86 nucleic acid sequence into an expression vector (column 8, lines 4-28 and Example 4, columns 30-33) and inserting the vector into a cell such as a COS cell (column 10, lines 33-47 and Example 5, column 33-34) for expression. The Examiner also stated that the reference provides oligonucleotides useful as diagnostic tools when labeled with a detectable marker (column 17, lines 27-35). The Examiner acknowledged that Freeman et al. does not specifically teach the nucleotide and corresponding amino acid sequence of feline CD86.

The Examiner asserts that it would have been obvious at the time the invention was made to utilize the methods disclosed by Freeman et al. (column 11, lines 50-62) to isolate the feline homologue of CD86. Therefore, it is the Examiner's position that the instant invention is obvious in view of Freeman et al.

Applicants maintain that the pending claims are not rendered obvious by the Freeman et al. reference. As the Examiner concedes on page 7 of the Office Action, Freeman et al. do "not specifically teach the nucleotide and corresponding amino acid sequence of feline CD86." Freeman et al. do not provide any nucleotide sequence information for any feline subject. Indeed, Freeman et al. do not disclose that such a nucleic acid encoding feline CD86 exists, let alone that such a nucleic acid is isolated and has a specific sequence. There is no disclosure of what the putative homology would be expected to be between the human CD86 sequence disclosed by Freeman et al. and the feline CD86. Freeman et al. provides neither the motivation nor an expectation of success for obtaining the feline homologue CD86.

In support of the rejection, the Examiner points out a passage in Freeman et al. (Column 11, lines 50-62) that allegedly describes methods to isolate feline CD86. This passage is merely a very general description that recites "isolation of cDNA clones from other species . . . using human cDNA inserts, such as B7-2 cDNA, as hybridization probes." There is no direction given by Freeman et al. as to which portion of such an insert to use as a hybridization probe. There is no direction or suggestion to look in felines, and there is no motivation to look in felines since the motivation given to perform such an isolation is based on isolating nucleic acids from a mammalian species which exhibits cross-reactivity with another species in order to modify T cell mediated immune responses. See column 11, lines 55-59. There is no information given about the cross-reactivity of feline T cells with other species. Again, there is no mention of feline at all. Therefore, Applicants maintain that the claimed invention, an isolated nucleic acid encoding a feline CD86 ligand or a feline soluble CD86 ligand,

wherein the nucleic acid is at least about 70% homologous with the nucleic acid shown in SEQ ID NO:5, would not be obvious to one of ordinary skill in the art in view of the Freeman et al. reference.

II. Rejection of Claims 2, 55 and 86-87

The Examiner rejected claims 2, 55 and 86-87 under 35 U.S.C. § 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 5,942,607) and Hash (Gene Bank Direct Submission, 8 May 1996).

The Examiner asserts that Freeman et al. teaches a fusion protein using B7-1 (CD80) and B7-2 (CD86), as well as the cloning of CD80 and CD86 as well as insertion of the nucleic acid sequences into expression vectors. The Examiner asserts that it therefore would have been obvious to one of ordinary skill in the art at the time the invention was made to use a CD80/CD86 fusion protein in order to use the protein as an immunomodulator.

Applicants traverse the rejection and maintain that the combination of Freeman et al. and Hash does not make obvious the claimed invention. The Freeman et al. reference is discussed supra. The disclosure of the Hash reference does not remedy the shortcomings of the Freeman et al. reference and the combination of Freeman et al. and Hash therefore is not sufficient to render the claimed invention obvious to one of ordinary skill in the art. Hash merely provides the sequence of feline CD80, which is not claimed or error mentioned in claim 2 or claim 55. Claims 86, 87 and 88, which have been canceled, include a reference to the feline CD80 nucleic acid; however, all of these claims depend from other claims that ultimately depend from claim 2. Applicants refer the Examiner to the discussion above regarding the Freeman et al. reference as

applied to claims 2 and 55. In brief, Freeman et al. relates only to the sequence of human CD86 and in no way teaches or suggests the presently claimed invention.

In view of the above discussion, reconsideration and withdrawal of these grounds for rejection is respectfully requested.

CONCLUSION

If a telephone conference would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.